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Review Article

Weight loss from lifestyle interventions and severity of sleep apnoea: a systematic review and meta-analysis

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ABSTRACT

Background: Excess body weight is a risk factor for obstructive sleep apnoea (OSA). The aim of the systematic review was to establish whether weight loss via lifestyle interventions such as diet and exercise are useful in the treatment of OSA.
Methods: A literature search was conducted between 1980 and February 2012. Systematic reviews and randomised controlled trials (RCTs) with participants who had OSA, were overweight or obese, and who had undergone lifestyle interventions with the aim of improving sleep apnoea were included. Meta analyses were conducted for a subset of RCTs with appropriate data.
Results: Two systematic reviews and eight RCTs were included. Meta-analyses were conducted for four RCTs comparing intensive lifestyle interventions to a control. The overall weighted mean differences for weight change, change in apnoea -hypopnoea index (AHI) and change in oxygen desaturation index of ≥4% were as follows: –13.76 kg (95% confidence interval (CI) –19.21, –-8.32), –16.09 (95% CI –25.64, –6.54) and –14.18 (95% CI –24.23, –4.13), respectively. Although high heterogeneity within the meta analyses, all studies favoured the interventions. Long-term follow-up data from three RCTs suggest that improvements in weight and AHI are maintained for up to 60 months.
Conclusions: Intensive lifestyle interventions are effective in the treatment of OSA, resulting in significant weight loss and a reduction in sleep apnoea severity. Weight loss via intensive lifestyle interventions could be encouraged as a treatment for mild to moderate OSA.

1. Introduction

Obstructive sleep apnoea (OSA) is characterised by repetitive episodes of upper airway obstruction, which can lead to a reduction in blood oxygen saturation and arousal from sleep [1]. OSA is strongly associated with central obesity and is independently associated with an increased risk of cardiovascular disease, hypertension, and stroke. In addition, OSA is associated with excessive daytime sleepiness, cognitive deterioration, motor vehicle accidents, and a reduction in quality of life [2]. OSA is estimated to affect 3–7% of men and 2–5% of women [3], with a predisposition in those who are male, middle-aged, overweight and with a family history of OSA [1,4]. It has been suggested that the true prevalence may be even higher, as undiagnosed OSA is common [5,6].

The most commonly used and effective management for OSA is the use of continuous positive airway pressure (CPAP) which acts as a pneumatic splint to maintain airway patency during sleep but relies on long-term adherence [7]. CPAP can result in nasal dryness and congestion, claustrophobia, facial skin abrasions, and conjunctivitis, all of which may affect compliance [8]. Similarly, the use of oral appliances to increase airway size during sleep is another possible management strategy. They are not as effective as CPAP therapy, but may lead to comparable health outcomes [9]. Weight loss via lifestyle modification or bariatric surgery may be effective treatments; however, the evidence for these is sparse [10].

Evidence is clear that excess body weight is a risk factor for OSA [4], with severity of symptoms generally increasing with body weight [1]. A recent review challenges the unidirectional relationship between obesity predisposing individuals towards airway collapse and development of sleep-disordered breathing, with the suggestion of a reciprocal relationship between obesity and OSA. This suggests that the metabolic derangement resultant from

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OSA contributes to either further weight gain or resistance to weight loss [11].

While weight reduction after the onset of the syndrome may lead to improvement of symptoms, this has not been conclusively shown [4]. Previous reviews of the effect of lifestyle intervention on OSA severity have been conducted, but have not included more recent randomised controlled trials (RCTs) in the area [12,13]. This systematic review aimed to evaluate the relationship between weight loss and severity of sleep apnoea to establish specifically whether weight loss via lifestyle interventions such as diet and exercise are useful in the treatment of OSA.

2. Methods

2.1. Data sources

To identify appropriate keywords, an initial limited search of MEDLINE was conducted, and the title, abstract and index terms used to describe the articles were reviewed. All identified keywords and index terms were used in the second search of Ovid MEDLINE, The Cochrane Library, EMBASE, CINAHL, Web of Science and Scopus. The reference lists of retrieved articles were also searched; however, no additional relevant studies were found.

2.2. Study selection

Keywords used were grouped into two main areas, those regarding sleep apnoea (apnea/apnoea, hypopnea/hypopnoea and OSA) and those concerning nutrition and physical activity interventions or weight loss (nutri*, diet, food, exercise, physical activity and weight). Keywords were agreed upon by the authors.

The review was limited to studies published between 1980 and February 2012, written in English, and conducted in humans. Studies with participants who had OSA, who were overweight or obese (body mass index (BMI) ≥ 25 kg/m^2 in Caucasian cohorts and BMI ≥ 23 kg/m^2 in Asian cohorts) and who had undergone lifestyle interventions with the aim of improving sleep apnoea were included if they reported both anthropometric and sleep apnoea outcomes. Studies where significant weight loss was not achieved were excluded, as were studies where weight loss occurred as a result of bariatric surgery or medications if it was not possible to separate results from other lifestyle interventions.

Once duplicates were removed, studies identified in the database search were assessed for relevance based on title and abstract. Studies meeting inclusion criteria were retrieved, as well as those for which it was uncertain. Initially, all study designs were included; however, as a sufficient number of systematic literature reviews and RCTs were identified, other study designs were later excluded. Levels of evidence were assigned using the National Health and Medical Research Council evidence tables [14].

2.3. Data extraction

Data were extracted using a developed data extraction form based on the Dietitians Association of Australia templates (LJM) [15]. Extracted information included populations (gender, age, BMI, OSA classification and co-morbidities), interventions (treatments provided and length of follow-up), comparators, sample sizes, outcomes, study designs, and funding sources. Extracted data were checked by an independent reviewer (ZED) and a consensus was reached where disagreement existed.

The quality of the included systematic reviews was first assessed using the American Dietetic Association criteria [16]. To determine the validity of included RCTs, studies were assessed for the adequacy of allocation randomisation and concealment, blinding of participants, personnel and outcome assessors and the completeness of outcome data reporting [17]. This was conducted by two independent reviewers (LJM and ZED) using the Cochrane Risk of Bias tool at the study level [17]. Criteria were discussed prior to assessment with disagreements resolved by consensus.

2.4. Results synthesis and statistical analysis

The relationship between weight loss from lifestyle intervention and severity of OSA was explored by meta-analysis. Firstly, weight changes were compared between those receiving the lifestyle intervention and those receiving control measures to demonstrate that the interventions were successful in achieving weight loss. Next, changes in the apnoea–hypopnoea index (AHI) and 4% oxygen desaturation index (ODI_4) between those receiving the lifestyle intervention and those receiving control measures were explored to determine the effect of weight loss on OSA severity.

Studies were included in the meta-analyses if they reported mean difference in weight, AHI and/or ODI_4 following the study period. Where data were reported in the format of baseline versus follow-up, the authors were contacted in order to obtain appropriate data points.

Analyses were undertaken using STATA (Version 11, StataCorp, 2009). The STATA *metan* command was used to calculate the overall WMD in weight, AHI and ODI_4 between those receiving the lifestyle intervention and those receiving control measures [18]. A random-effects model was used whereby the WMD was calculated and is reported as WMD (95% confidence interval (CI)). Heterogeneity was examined both qualitatively and quantitatively using the I^2 statistic: low heterogeneity is defined as <25%, medium as <50% and high as <75% [19].

Studies not included in the meta-analysis were evaluated and summarised qualitatively.

2.5. Follow-up data

Several of the included studies published additional follow-up data. These publications were identified and assessed for quality. Data were then extracted and included within the qualitative summary of results.

3. Results

3.1. Included studies

The search identified 3622 articles, 12 of which were included in the final review (Fig. 1). In addition, three articles reporting follow-up data were identified subsequent to the initial search. The two systematic reviews that met the inclusion criteria are outlined in Table 1. Both systematic reviews included weight loss via dietary means and its impact on OSA, one of neutral quality [13] and one of poor quality [20]. These systematic reviews both showed positive effects of weight loss on OSA; however, only two of 11 included studies were RCTs. A third systematic review which assessed weight loss, sleep hygiene or exercise programs versus placebo was retrieved; however, it was subsequently excluded because no studies met the review's strict inclusion criteria [12].

Thirteen publications from eight different RCTs were identified, with two of these being reported in the included systematic reviews [21,22]. The characteristics of the included publications are described in Table 2, while the results are reported in Table 3. Follow-up data were reported for three of the RCTs. Specifically, follow-up data from Kemppainen et al. [27] and Tuomilehto et al. [31] were reported at 24 and 60 months [32,33]; follow-up data from Foster [24] were reported at 24 and 48 months [28];

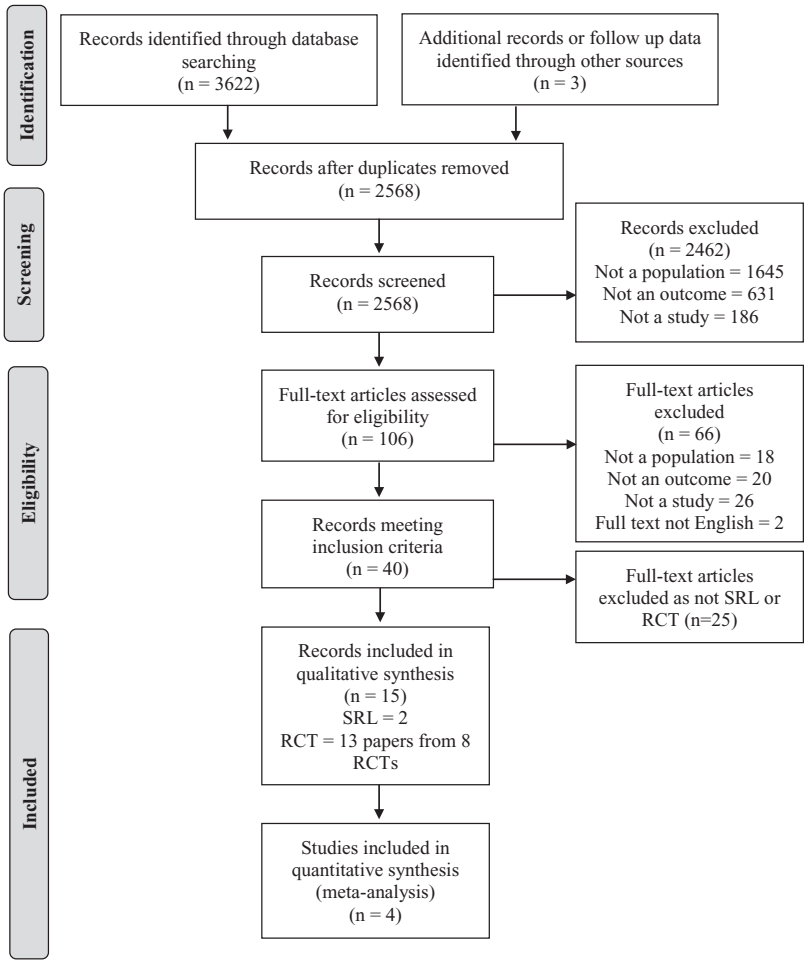

Fig. 1. Identifying studies for inclusion. SRL = systematic review of the literature; RCT = randomised controlled trial.

and follow-up data from Johansson et al. [25] were reported at 12 months [26]. Overall, the eight RCTs included 618 participants. All studies were assessed using the Cochrane Risk of Bias tool (Figs 2 and 3).

3.2. Quantitative study synthesis

Nine articles from four different RCTs assessed the impact of intensive lifestyle intervention compared with conservative lifestyle intervention [24,27,28,31–33], usual diet [22,25,26] or a weight maintenance control [30] on sleep apnoea outcomes and so were eligible to be included in the meta-analyses. Only those studies reporting the immediate effect of the intervention were included in the meta-analysis. Follow-up studies could not be included in the meta-analysis as this would be including multiple data points for the same study. For one RCT, data were reported at 12 weeks (following very low-calorie diet intervention) [27] and at 12 months following the active maintenance period of the intervention [31]. Only the 12-month data were included in the meta-analysis as it assessed the entire intervention period [31].

3.2.1. Weight

Four studies were included in the meta-analysis assessing the effect of intensive lifestyle interventions on weight change (Fig. 4). Time frames for the interventions varied with two of the studies being only short-term interventions (8 weeks [30] and 9 weeks [25]) while two showed the impact of a 12-month intervention [24,31]. Foster et al. [24] and Tuomilehto et al. [31] compared intensive lifestyle intervention to conservative lifestyle intervention, whilst Johansson et al. [25] compared it with usual diet, and Nerfeldt et al. [30] with a weight maintenance control. The WMD for weight was –13.76 kg (95% CI –19.21, –8.32) demonstrating that the interventions were successful in achieving weight loss over the study period. Despite the high degree of heterogeneity ($I^2 = 95.7\%$), in all studies the interventions produced weight loss. The studies included in the meta-analyses generally showed a lower risk of bias.

3.2.2. Apnoea–hypopnoea index

Four studies were included in the meta-analysis evaluating the effect of intensive lifestyle intervention on AHI (Fig. 5) [24,25,30,31]. The WMD for AHI was –16.09 (95% CI –25.64, –6.54); however, this sample was again highly heterogeneous ($I^2 = 92.2\%$). Sensitivity analysis was conducted to determine if outcomes differed when using the 12-week data [27], rather than the 12-month data of the study with different time points [31]. This analysis showed similar results (WMD = –15.76 (95% CI –26.45, –5.06), $I^2 = 92.7\%$).

3.2.3. Oxygen desaturation index

Three studies were included in the meta-analysis evaluating the effect of intensive lifestyle intervention on ODI_4 (Fig. 6) [24,25,30]. The overall ODI_4 WMD was –14.18 (95% CI –24.23, –4.13) and again this sample was highly heterogeneous ($I^2 = 83.5\%$).

Table 1
Systematic review study characteristics.

Citation	Study design	Level of Evidence	Population characteristics	Intervention and comparator	Sample size	Length of follow up	Outcome(s) measured	Quality [15]	Results
Veasey 2006 [13]	Systematic review of two RCTs (Smith 1985 [22], Kajaste 2004 [21]), four non-randomised two-arm intervention studies (Rauscher 1993 [38], Schwartz 1991 [39], Nahmias 1993 [40], Noseda 1996 [41]), one case – control study (Kansanen 1998 [42]), two single-arm intervention studies (Lojander 1998 [43], Sampol 1998 [44]), two cohort studies (Peppard 2000 [45], Fisher 2002 [46])	Level II to IV	Adults with OSA	Weight loss vs baseline, CPAP, or usual care	Not stated	Not stated	AHI, oxyhaemoglobin desaturation index	Neutral – Only one database searched, studies not described well, no quality analysis, unsure how many people extracted data/reproduced. Included: search terms, inclusion/exclusion criteria, evidence level identified.	Overall, weight reduction was associated with reductions in the AHI for reduced calorie therapies. Most identified studies that reported weight loss effects on OSA lacked control groups, randomised design, or sufficiently high alpha and beta error to provide strong support for clinical practice guidelines. Moreover, few studies have examined the long-term effects of weight loss therapies on OSA. In summary, studies to date demonstrate that weight loss, achieved by dietary modification, can occur and can be significant.
Strobel 1996 [20]	Systematic review of one RCT (Smith 1985 [22]), 3 two-arm interventions (Schwartz 1991 [39], Suratt 1992 [47], Nahmias 1993), three single-arm interventions (Rubinstein 1988 [48], Pasquali 1990 [49], Kiselak 1993 [50]), one cohort (Rajala 1991 [51])	Level IV	Not described	Weight loss via dietary instruction, very low calorie diet, diet + behavioural therapy versus baseline or no therapy	142	4.5–24 months	Improvement in sleep-disordered breathing, oxygen haemoglobin saturation, sleep fragmentation, daytime performance, upper airway function, airway structure, load response, ventilary drive	Negative – Only one database searched, no quality analysis, did not consider level of evidence, unknown how many investigators extracted data, data extraction and collation not described. Search terms described.	There is accumulating evidence of the value of dietary weight loss in the treatment of obese patients with OSA. Although the amount of weight loss achieved has varied widely from one report to another, positive treatment effects on shortness of breath and sleep quality have been reported in all but one study to date.

Levels of evidence assigned using the National Health and Medical Council evidence table [14].
Abbreviations: OSA = Obstructive Sleep Apnoea; CPAP = continuous positive airway pressure; AHI = apnoea–hypopnoea index; COPD = chronic obstructive pulmonary disease; RCT = randomised controlled trial.

Table 2
RCT Study Characteristics.

Study	N (a/b)	Population characteristics	Setting	Intervention length	Intervention
Chakravorty 2002 [23]	32/21	AHI ≥ 15. Mean(SD): age 50(11); BMI 37(12); ESS score 14(5); AHI 49.	UK	3 months	a) CPAP therapy b) conservative lifestyle intervention
Foster 2009 [24][1]	125/139	45–75 years; BMI > 25; type 2 diabetes; AHI ≥ 5; no previous surgical or current medical treatment for OSA. Mean (SD): age 61.3(6.5); BMI 36.7(5.7). 41% male	USA	12 month	a) Intensive lifestyle intervention: group behavioural weight loss. Prescribed portion-controlled diets (liquid meal supplements, frozen entrees and snack bars for 0–4 months, reduced over subsequent 8 months). Prescribed 175 min/week moderate-intensity physical activity. b) Three group sessions over the 1-year period, focusing on diet, physical activity and social support related to diabetes management
Johansson 2009 [25][2]	30/33	Males; 30–65 years; BMI 30–40; moderate to severe OSA (AHI ≥ 15); treated with CPAP for >6 months. Mean (SD): age 49(7.3); AHI 37(15); 100% male	Sweden	9 weeks	a) Weight loss program beginning with a 7-week VLCD (providing 2.3 MJ/d), then 2 weeks of gradual introduction of normal foods to reach 6.3 MJ/d, with group sessions every 2 weeks b) Usual diet (received intervention after 9 weeks)
Johansson 2011 [26][2]	63	Males; 30–65 years; BMI 30–40; moderate to severe OSA (AHI ≥ 15); treated with CPAP for >6 months. Mean (SD): age 49(7.3); AHI 36(15); 100% male	Sweden	12 months	a) 9-week intensive weight loss program (7-week VLCD providing 2.3 MJ/d, then 2 weeks of gradual introduction of normal foods to reach 6.3 MJ/d, with group sessions every 2 weeks) followed by maintenance program (monthly group therapy meetings in conjunction with individual dietetic consultation). In the event, a patient regained >2 kg in the previous month, partial meal replacements and orlistat or sibutramine were used as primary and secondary strategies, respectively, Group includes those patients ($n = 33$) randomised to follow a usual diet for 9 weeks before completing the 12-month intervention (intensive weight loss program + weight maintenance program).
Kajaste (2004) [21] (included in Veasey 2006 [13])	17/14	Males; 30–60 years; BMI ≥ 35; subjective symptoms of OSA; ODI4 >10; 100% male	Finland	24-month intervention; 36-month follow-up	a) 6-week VLCD + 24-month cognitive behavioural therapy + 6 months CPAP b) 6-week VLCD + 24-month cognitive behavioural therapy + no CPAP
Kemppainen 2008 [27][3]	26/26	18–65 years; BMI 28–40; mild OSA (AHI: 5–15/h); 79% male	Finland	12-week intervention	a) 12-week personalised VLCD b) general diet and exercise information
Kuna 2013 [28][1]	125/139	45–75 years; BMI > 25; type 2 diabetes; AHI ≥ 5; no previous surgical or current medical treatment for OSA. Mean (SD): age 61.3(6.5); BMI 36.7(5.7). 41% male	USA	48 months	a) Intensive lifestyle intervention: group behavioural weight loss. Prescribed portion-controlled diets (liquid meal supplements, frozen entrees and snack bars for 0–4 months, reduced over subsequent 8 months). Prescribed 175 min/week moderate-intensity physical activity. For remainder of intervention period, (year 2 through 4) individual advice provided monthly with at least one on site visit and one other contact (telephone, email, mail). b) Three group sessions annually, focusing on diet, physical activity and social support related to diabetes management
Lam 2007 [29]	34/34/33	AHI ≥ 5–40; Epworth Sleepiness Scale (ESS) > 9 for those with AHI 5–20; no BMI, age or gender requirement. Mean(SD): AHI 21.4(1.1); 87% male	China	10 weeks	a) conservative measures (advice for general sleep hygiene, overweight subjects asked to attend a weight control program) + CPAP b) conservative measures + oral appliance c) conservative measures
Nerfeldt 2008 [30]	6/5	Males; 20–69 years; BMI ≥ 30; AHI ≥ 10 and/or ODI ≥ 6; subjective symptoms of OSA. Median (range): age 51(35–69); BMI 36(30–40); 100% male	Sweden	8-week intervention, then crossover	a) 8-week LCD + group meetings once/week b) weight maintenance control (crossover after 8 weeks)
Smith 1985 [22] (included in Veasey 2006 [13] and Strobel 1996 [20])	15/8	Documented sleep apnoea; hypersomnolence; no BMI or age requirement; 83% male	USA	Seen every 2–3 months until: a) ≥ 5% weight loss; b) ≥ 1 month weight stable	a) weight loss (reduced calorie intake to aim for 0.45–0.9 kg/week). No specific diets, medications, or behavioural modification b) weight stable control
Tuomilehto 2009 [31][3]	35/37	18–65 years; BMI 28–40; mild OSA (AHI: 5–15/h); 74% male	Finland	12 months	a) 12-week personalised VLCD followed by 1-year lifestyle intervention program (14 dietary counselling consultations) b) general diet and exercise information
Tuomilehto 2010 [32][3]	35/36	18–65 years; BMI 28–40; mild OSA (AHI: 5–15/h); 75% male	Finland	12-month intervention; 24-month follow-up	a) 12-week personalised VLCD followed by 1-year maintenance program (14 dietary counselling consultations) b) general diet and exercise information
Tuomilehto 2013 [33][3]	28/29	18–65 years; BMI 28–40; mild OSA (AHI: 5–15/h)	Finland	12-month intervention; 60-month follow-up	a) 12-week personalised VLCD followed by 1-year maintenance program (14 dietary counselling consultations) b) general diet and exercise information

N(a/b) = number of participants in group a and b (refer to 'Intervention' column). All studies are RCT – parallel (Level II) as per the National Health and Medical Council evidence table [14].

[1,2,3] Superscript numbers identify multiple publications reporting follow-up from one RCT.

Abbreviations: AHI = apnoea–hypopnoea index; BMI = body mass index; ESS Epworth Sleepiness Scale; CPAP = continuous positive airway pressure; LCD = low-calorie diet; VLCD = very low-calorie diet.

Table 3
Changes in body weight and OSA markers over time, intervention versus control.

Study	Time period	Group	Weight (kg)	BMI (kg/m^2)	Waist circumference (cm)	AHI	ODI4	ESS	Cured patients, *N* (%)	Correlations
Chakravorty 2002 [23]	baseline versus 3 months	a)		40(14.5) versus 40(12.8), ns	–	55(28.7) versus 8(28)	–	16(5.6) versus 8(6.4)		–
		b)		32.3(5.5) versus 31.7(5.6)	–	35(19.1) versus 34(21)	–	14(4.2) versus 11(5)		–
Foster 2009 [24][1]	baseline–12-month changes	a)	–10.8(7.8)	–3.8(3.4)	–9.3(7.8)	–5.4(16.8)	–5.5(15.7)	–		Weight and AHI: $r = 0.35$
		b)	0.6(8.3)	–0.2(3.5)	–0.5(7.1)	4.2(16.5)	1.2(15.3)	–		
Johansson 2009 [25][2]	baseline–9 weeks changes	a)	–18.7(4.1)	–5.7(1.1)	mean difference between groups: –17.7 (19.1 to 16.3)	–25(17)	–19(14)	–3(5)		
		b)	1.1(1.9)	0.3(0.6)		–2(11)	–1(9)	1(3)		
Johansson 2011 [26][2]	baseline–12 month changes	a)	–12.1(9.0)	–3.7(2.7)	–12.8(8.5)	–17(16)	–13(13)	–2(3)	6(10)	AHI and weight: $r = 0.41$; AHI and waist circumference: $r = 0.40$
Kajaste 2004 [21]	Baseline versus 6 months	a)	135.3(16.0) versus 116.2(16.3)	42.5 (4.5) versus 36.6 (5.2)	–	–	–29.5(27.0)	–	–	ODI_4 and weight in all patients: 0.59 at 6 months; 0.68 at 12 months; 0.75 at 24 months
		b)	145.5 (23.4) versus 126.3 (27.0)	45.4 (6.2) versus 39.4 (7.7)	–	–	–26.3(21.2)	–	–	
Kemppainen 2008 [27][3]	baseline–3 months changes	a)	–	–5.4	–	–3.2(9.2)	–	–		AHI and BMI: $r = 0.302$
		b)	–	–0.5	–	–1.3(5.5)	–	–		
Kuna 2013 [28][1]	baseline–24-month changes	a)	–7.4(7.8)	–	–5.99(7.71)	–3.8(16.8)	–	–		
		b)	–0.8(8.3)	–	–0.71(7.78)	4.2(16.5)	–	–		
	baseline–48-month changes	a)	–5.2(7.8)	–	–3.42(7.94)	–4.0(17.9)	–	–	20.7%	
		b)	–0.8(8.3)	–	0.17(8.02)	3.7(18.9)	–	–	3.6%	
Lam 2007 [29]	Baseline versus 10 weeks	a)	75.8(9.9) versus 74.6(9.3)	27.6(3.5) versus 27.2(3.5)	–	23.8(11.1) versus 2.8(6.4)	–	12(5.8) versus 7(5.8)	–	Changes in AHI (without device) and body weight: $r = 0.298$
		b)	73.3(11.1) versus 72.3(12.8)	27.3(3.5) versus 26.9(3.5)	–	20.9(9.9) versus 10.6(9.9)	–	12(5.8) versus 9(5.8)	–	
		c)	74.8(13.2) versus 74.5(12.6)	27.3(3.4) versus 27.1(3.4)	–	19.3(10.9) versus 20.5(14.4)	–	12(5.7) versus 10(5.7)	–	
Nerfeldt 2008 [30][a]	baseline–8-week changes	a)	–14.8(3.4)	37(33–40) versus 32.2(27.8–35.2)[b]	–	–25.5 (9.9)	–29.5(21.8)	–		
		b)	0.6(2.1)	33.1 (30.2–36.4) versus 32.6(30.9–36.7)[b]	–	7.8 (10.7)	–5.8(7.3)	–		
Smith 1985 [22]	a) ≥5% weight loss; b) ≥1 month weight stable	a)	106.2(28.3) versus 96.6(22.9)	–	–	–	–	–	–	Decreased weight and improved apnoea frequency: $r = 0.0345$
		b)	118.8(20.9) versus 120.2(23.5)	–	–	–	–	–	–	
Tuomilehto 2009 [31][3]	baseline–12-month changes	a)	–10.7(6.5)	–3.5(2.1)	–11.6(6.6)	–4.0(5.6)	–	–3.1(4.0)	22(63)	
		b)	–2.4(5.6)	–0.8(2.0)	–3.0(6.0)	0.3(8.0)	–	–2.1(2.9)	13(35)	
Tuomilehto 2010 [32][3]	baseline–24-month changes	a)	–7.3(6.5)	–2.4(2.1)	–7.7(6.7)	–4.6(4.9)	–	–2.3(3.6)	20(57)	
		b)	–2.9(7.5)	–1.0(2.6)	–3.5(7.3)	–0.5(9.3)	–	–2.9(4.4)	11(31)	
Tuomilehto 2013 [33][3]	baseline–60-month changes	a)	–5.5(7.5)	–1.9(2.4)	–4.6(7.6)	–0.8(6.5)	–	–	9(32)	
		b)	0.6(8.5)	0.2(3.0)	0.8(8.6)	5.0(10.9)	–	–	5(17)	

Group a) and b) as per Table 2. Dashes (–) indicate outcomes not measured.
Abbreviations: AHI = apnoea–hypopnoea index; ODI_4 = oxygen desaturation index ≥4%/h of sleep; OAI = obstructive apnoea index; ESS = Epworth Sleepiness Scale.
[a] Data presented as baseline and 8 weeks in paper. Contacted author to obtain mean (SD) change as well as AHI results.
[b] Median (range).
[1,2,3] Superscript numbers identify multiple publications reporting follow-up from one RCT.

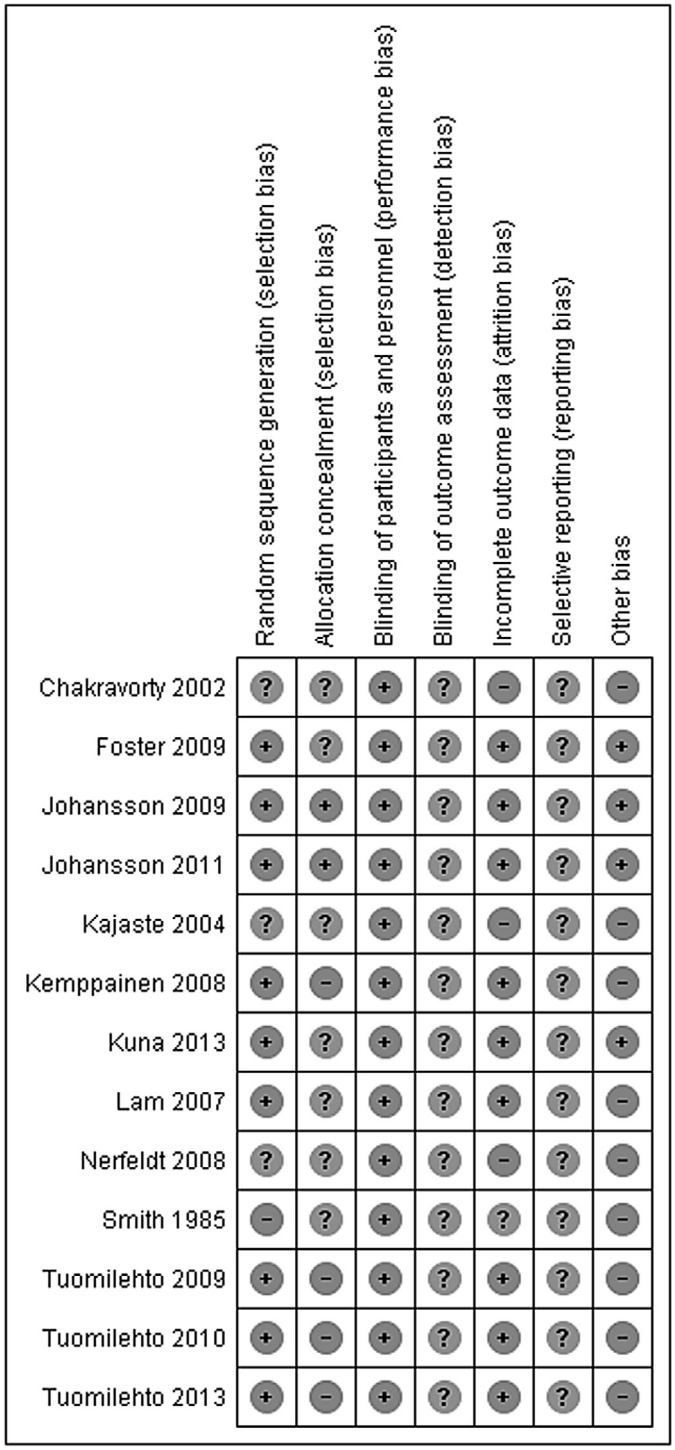

Fig. 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study. + indicates low risk of bias; – indicates high risk of bias; ? indicates unclear risk of bias in each respective aspect of study design.

3.3. Qualitative study synthesis

The impact of intensive lifestyle intervention on the Epworth Sleepiness Scale (ESS) was reported in two studies, one comparing it to conservative lifestyle intervention [31] and one with usual diet [25]; however, this was not assessed in a meta-analysis. While both these studies showed a similar improvement in the intervention group, the change in the control group differed and the standard deviations were reasonably wide limiting the conclusions that can be drawn from the data (the Tuomilehto et al. intervention: –3.1 ± 4; conservative control: –2.1 ± 2.9 [31]; the Johansson et al. intervention: –3 ± 5; and usual diet control: 1 ± 3 [25]).

While Smith et al. compared a weight loss group achieving significant weight loss with a weight maintenance control group, the RCT could not be included in the meta-analysis as it was of poor quality and did not report the key measures of sleep apnoea [22]. It did, however, show a reduction in apnoea frequency.

Three RCTs were not able to be included in the meta-analysis as they assessed the effect of CPAP as the distinguishing factor rather than intensive lifestyle intervention. Chakravorty et al. compared CPAP with conservative lifestyle intervention [23]. Conservative lifestyle intervention was able to achieve a significant reduction in BMI, while the CPAP group was not. Despite this, the CPAP group achieved significant improvements in AHI and ESS, while conservative lifestyle measures were able to significantly improve ESS, but not AHI. Kajaste et al. compared intensive lifestyle intervention with CPAP with intensive lifestyle intervention with no CPAP [21]. This study showed significant changes in both groups in the measured outcomes of weight, BMI and ODI_4. Lam et al. evaluated conservative lifestyle intervention plus CPAP or oral appliance with conservative measures on its own [29]. The conservative intervention included the overweight subjects in the group being referred to a weight control program ($n = 84/101$). While weight loss was not clinically significant between groups, only the participants in the conservative lifestyle intervention plus the CPAP group were able to achieve statistically significant weight loss. Both CPAP and the oral device were able to significantly improve AHI and ESS compared with conservative measures on their own.

Reviewing the follow-up data published by several of the included RCTs, improvements in both weight, and AHI following lifestyle interventions with weight loss appear to be maintained. Considering the most recent follow-up data, Tuomilehto et al. demonstrate a significant difference in weight change and AHI change between intervention and control groups at 60 months [33]; Johannson et al. demonstrate a significant difference in weight and AHI compared with baseline at 12 months [26]; and Kuna et al. demonstrate a significant difference in weight change and AHI change both between groups and compared with baseline at 48 months [28].

4. Discussion

This systematic review brings together a variety of research to evaluate the relationship between weight loss from lifestyle intervention and severity of OSA. While systematic reviews have been conducted in the area of sleep apnoea and weight loss via lifestyle interventions, these reviews are not recent and are limited by their neutral/poor quality and lack of included RCTs. However, the results from this systematic review are consistent with the systematic reviews by Veasey et al. [13] and Strobel and Rosen [20], which show that weight loss can occur as a result of lifestyle interventions and consequently can improve sleep apnoea severity.

Overall, the RCTs that compared the impact of intensive lifestyle interventions with a control group show that a clinically and statistically significant weight loss can be achieved by the intervention. Typical lifestyle intervention involved portion-controlled low-energy diets as well as recommendations to increase daily exercise and activity. These interventions were usually coupled with ongoing intensive support from health professionals, via individual and group counselling, to provide motivation and maintain dietary compliance. Concurrent with weight loss, there were improvements in the key markers of sleep apnoea, such as AHI and ODI4, thus supporting weight loss by lifestyle intervention as a sole or concurrent treatment for OSA. It should be noted, however, that

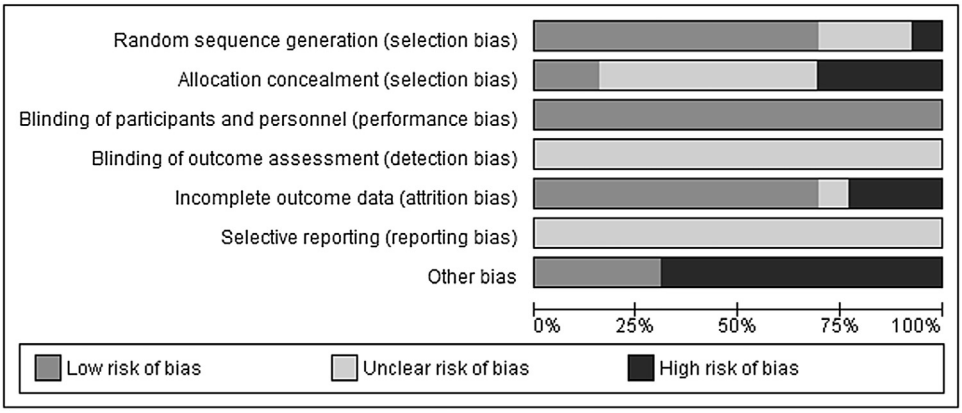

Fig. 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies. The bars represent the proportion of studies with low, high or unclear risk of bias in each respective aspect of study design.

despite the improvement in OSA severity, AHI was reduced to the normal range (AHI < 5/h) in only a minority of participants in the RCTs.

Only two trials specifically reported on the proportion of patients objectively cured of OSA (AHI < 5). In the 12-month follow-up by Johannson et al., 10% of participants had total remission of OSA after a 9-week lifestyle intervention with weight loss [26]. Also at 12 months, Tuomilehto et al. reported that 63% of participants who had successfully lost weight were objectively cured of OSA compared with 35% of the control group receiving general diet and exercise information ($p = 0.019$) [31]. These figures were maintained at the 24-month follow-up (57% vs. 31%, respectively; $p = 0.032$), but not at the 60-month follow up (32% vs. 17%, respectively; $p = 0.43$) [32,33]. Tuomilehto et al. also assessed the incidence of progression of OSA. At 60 months, there was a 61% reduction in the progression of the OSA in the intervention group compared with the control group ($p = 0.04$) [33]. Only patients with mild OSA (AHI: 5–15) were recruited for this study, so it is unclear if lifestyle intervention with weight loss can objectively cure those with moderate to severe OSA.

The change in severity of OSA based on AHI could only be assessed at an aggregate level in four studies included in the reviews. Of these, three studies demonstrated improvements *within* OSA classifications only, that is, improvements within the mild classification [27], moderate classification [24] and severe classification [23]. However, in the study by Johansson et al., participants experienced an average reduction in AHI of 25 events/h from a baseline average of 37 event/h [25]. At this crude level, this would have shifted the severity of OSA in this group from severe to mild. Theoretically, the meta-analysis determined that AHI improved by an average of –16.09 events/h in the included studies; however, given the heterogeneity present in the summary effect, this result cannot be applied to all populations. Understanding who is responding to the lifestyle intervention, in terms of both weight loss and OSA

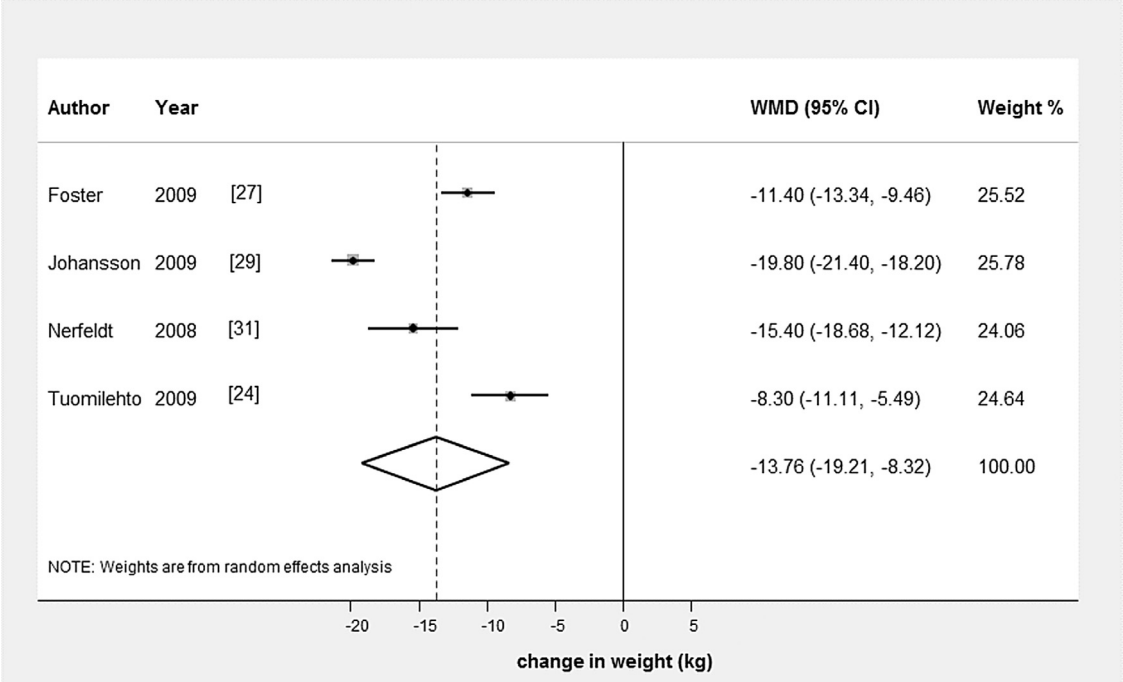

Fig. 4. Meta-analysis for weight change as a result of Intensive Lifestyle Intervention compared with control. $I^2 = 95.7\%$; test of WMD = 0: $z = 4.96$, $p = 0.000$.

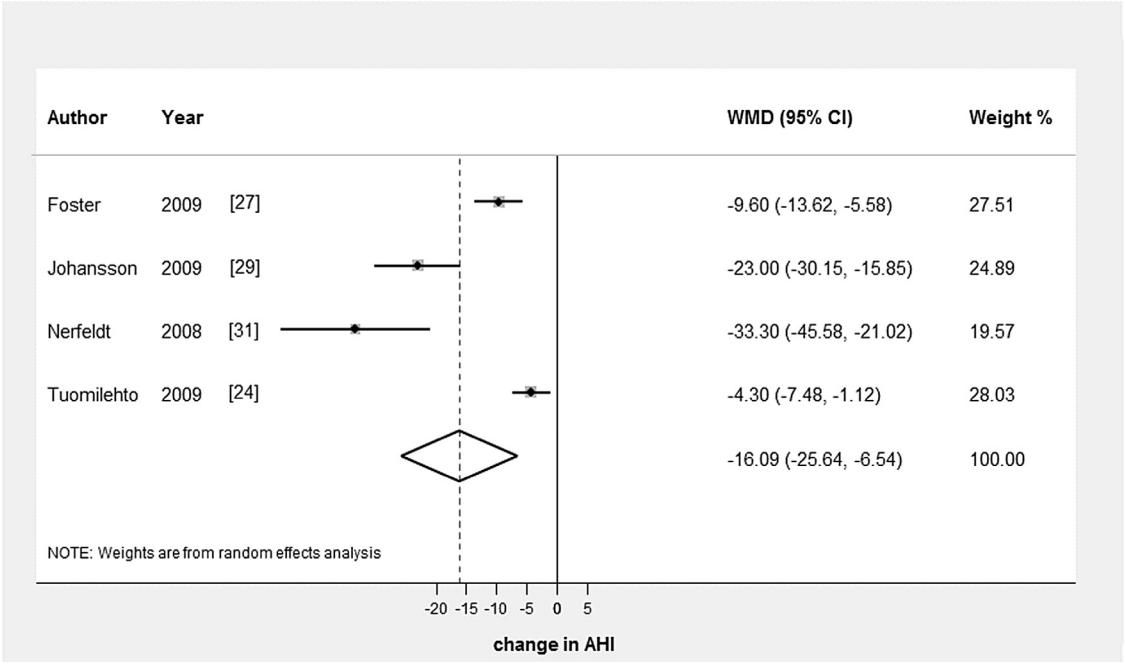

Fig. 5. Meta-analysis of change in Apnoea–Hypopnoea Index (AHI) as a result of Intensive Lifestyle Intervention compared with control. $I^2 = 92.2\%$; test of WMD = 0: $z = 3.30$, $p = 0.001$.

improvement, and the interaction between these two factors would be a worthy avenue for future research.

There are several limitations of this analysis. Firstly, while some lifestyle interventions may have included those focusing on physical activity, those which did not result in significant weight loss were not included in this review. However, it is of interest to note that in some studies assessing physical activity interventions, markers of sleep apnoea were significantly improved in intervention groups compared with controls [34,35]. Kline et al. [34] showed that doing 150 min/week moderate-intensity aerobic activity and resistance training 2×/week resulted in significant decreases in AHI and ODI_4 compared with stretching, which actually increased such indices. Similarly, in a study by Sengul et al. [35], AHI also significantly decreased with exercise training (15–30 min of breathing exercises, 45–60 min of aerobic exercises 3×/week for 12 weeks), while it remained the same for the control group. However, the reductions in AHI in the studies by Kline et al. [34] and Sengul et al. [35] (7.6 and ~4, respectively) were considerably less than that demonstrated by our meta-analysis (16.1).

Rissanen et al. [36] propose that exercise interventions may be beneficial for patients with sleep apnoea not only because of potential weight loss but also because it stimulates the respiratory drive.

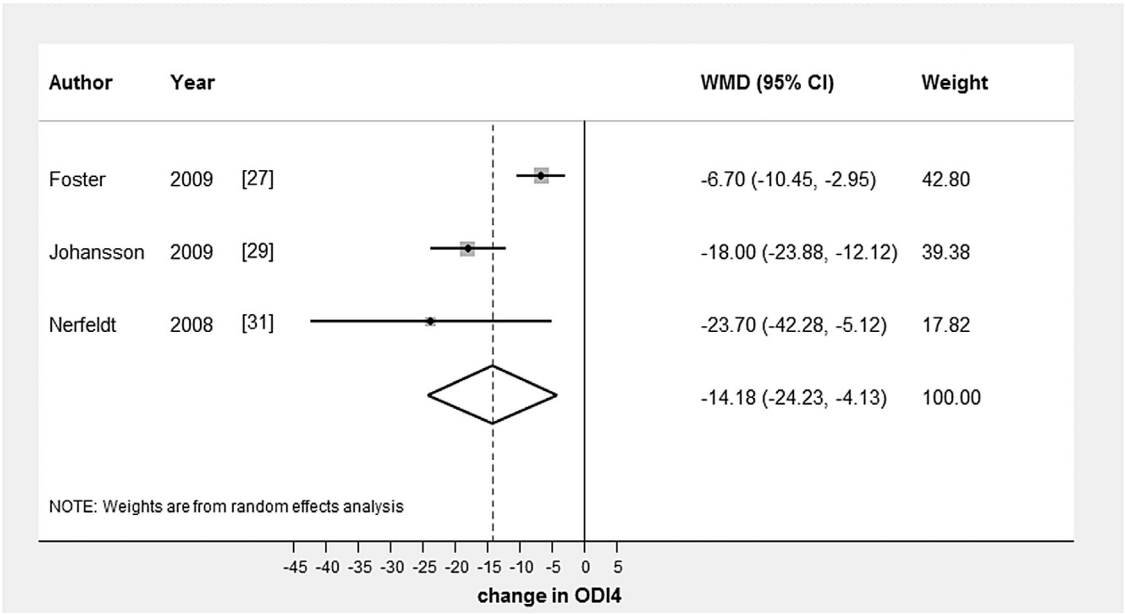

Fig. 6. Meta-analysis of change in Oxygen Desaturation Index ≥4% as a result of Intensive Lifestyle Intervention compared with control. $I^2 = 83.5\%$; test of WMD = 0: $z = 2.76$, $p = 0.006$.

For interest, the meta-analysis that explored change in AHI was conducted again including the study by Kline et al. [34] despite this group not experiencing weight loss (there were insufficient data points in the study by Sengul et al. [35] to be included). Although the change in AHI following lifestyle intervention remained significant, inclusion of a study where weight loss was not achieved weakened the effect on AHI. Specifically, the WMD in AHI reduced from –16.09 (95% CI –25.64, –6.54) to –15.07 (95% CI –22.80, –7.33). Therefore, it appears that lifestyle interventions that induce weight loss may offer additional benefits than those that do not. It is possible that dietary weight loss combined with an exercise program would have an even greater positive effect on OSA compared with those utilising dietary intervention alone. Future research should focus on combining weight loss interventions with frequent exercise to determine if such a program would indeed result in greater improvements in AHI.

Heterogeneity of the samples is also an evident limitation of these analyses; however, this is expected considering the varied time frames of the RCTs and variations in control groups. Regardless of this, all studies consistently reported favourable outcomes, just to varying degrees. Another limitation is the failure of many of the included studies to use an intention-to-treat analysis which may have biased the results. The small sample size of many of the studies is also a limitation.

It is important to note that the majority of the participants in these studies were males, with 4/12 RCTs recruiting only men and an additional 5/12 having >75% males. Whilst this preference for recruiting males in the sampling is due to the higher incidence of OSA in males [37], this will limit the generalisability of these findings. The smaller presence of females may have also contributed to the high degree of heterogeneity across the meta-analyses.

To conclude, intensive lifestyle interventions are effective in the treatment of OSA, resulting in significant weight loss and a reduction in OSA severity. Therefore, weight loss via intensive lifestyle interventions could be encouraged as a first-line treatment for mild to moderate OSA, either in isolation or in combination with other sleep apnoea management strategies. Future research directly comparing lifestyle interventions with sleep devices would be beneficial. Intensive lifestyle interventions could provide a cost-effective alternative to CPAP and oral devices, as well as potentially lead to greater improvements in metabolic health. Additional research is needed to establish whether significant weight loss combined with physical activity interventions would prove to be even more effective in managing OSA.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.05.012.

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